# Naval Medical Center Portsmouth (NMCP) COVID-19 Literature Report #87: Friday, 18 February 2022

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**Purpose:** These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers. Please reach out with questions, suggestions for future topics, or any other feedback. If this report made a difference or impacted patient care, please let me know!

All reports are available online at <a href="https://nmcp.libguides.com/covidreport">https://nmcp.libguides.com/covidreport</a>. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Due to the rapid evolution of the literature, I will not update past reports when new information arises; for retracted papers specific to COVID-19, see the list of retracted papers from Retraction Watch.

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# The Big Picture

## News in Brief

2 years in to the pandemic, *Scientific American* has a special report with numerous articles on how COVID changed the world (<u>SciAm</u>).

#### Data

"U.S. 'excess deaths' during pandemic surpassed 1 million, with covid killing most but other diseases adding to the toll, CDC says" (WP).

Meanwhile, the US is on the cusp of hitting 1 million deaths due to covid; as of this writing, the CDC shows 926,497 total deaths from covid (CDC).

"Covid deaths highest in a year as omicron targets the unvaccinated and elderly" (WP).

"Biden officials trying to recalculate U.S. Covid-19 hospitalizations" (Politico).

#### Pandemic Fallout

"Paying bills or buying masks: Simple living with COVID is hitting some Americans hard" (NPR).

"Africa may have been hit harder by covid-19 than anyone knew" (WP).

After 2 years of closed borders, Australia will allow fully vaccinated travelers in starting later this month (NPR).

## **Preparedness**

"U.S. officials prepare for pandemic's next phase as Omicron wanes" (Reuters).

"The next pandemic could start with a terrorist attack" (Atlantic).

## Long Reads

"We're entering the control phase of the pandemic. The virus isn't done with us. So we need a new approach to dealing with it" (Atlantic).

"How medicine must change for endemic COVID-19" (Boston Review).

Podcast: "What people get wrong about endemic COVID" (Nature).

## Webinars and Upcoming Events

WHAT: Around The Table: The Impact Of COVID-19 On The Future Of Medical Education

presented by New York Academy of Medicine

WHEN: virtual; Monday, 28 February 2022 1200–1245 ET

**DETAILS:** 

"Our first 2022 Around the Table discussion will focus on how the lessons learned from COVID-19 will shape the way we teach our medical students and guide physicians in the future. Drs. Salerno and Riley will be joined by Catherine R. Lucey, MD, MACP, Vice Dean for Education and Executive Vice Dean for the School of Medicine at the University of California, San Francisco (UCSF). In her career, Dr. Lucey has worked to influence both the direction and the continuum of medical education. Dr. Lucey will provide perspectives on the lessons already learned from the pandemic and how their application will provide a way forward."

MORE INFO: <a href="https://www.nyam.org/events/event/around-table-impact-covid-19-future-">https://www.nyam.org/events/event/around-table-impact-covid-19-future-</a>

medical-education

#### **Journal Articles**

Am J Infect Control: <u>Global analysis of the COVID-19 research landscape and scientific impact</u> (02 January 2022)

"Objectives: To consider a one-year time window of the COVID-19 crisis to integrate qualitative and quantitative data and provide an in-depth analysis of all COVID-19 publications from geographical, epidemiological and chronological perspectives.

Methods: Publications on COVID-19 from December 1, 2019, to December 31, 2020 without document type limitations were extracted from the Web of Science database. Microsoft Excel 2016, GraphPad Prism 9, VOSviewer 1.6.15 and IBM SPSS 21.0 were used to analyze the global epidemiological publication landscape and its correlations, research hotspots around the world and the top 5 countries in terms of publications.

Results: A total of 51,317 documents were analyzed in the present study. The publication trend could be divided into an increasing output stage and an explosive output stage. There were positive correlations between monthly publications, confirmed cases and deaths.

Research hotspots from the whole year, from individual quarters, and from the top 5 countries with the most publications were further identified.

Conclusions: The correlation analysis of publications indicated that confirmed cases and deaths were forces driving the scientific output, reflecting the growing trend to some extent. Moreover, the hotspot analysis provided valuable information for scientists, funders, policy and decision-makers to determine what areas should be their focus when faced with public health emergencies in the future."

#### **SARS-CoV-2 Virus and Variants**

## News in Brief

"Coronaviruses are 'clever': Evolutionary scenarios for the future of SARS-CoV-2" (STAT).

"We regret to inform you that we are now discussing subvariants" (Vox).

"As BA.2 subvariant of Omicron rises, lab studies point to signs of severity" (<u>CNN</u>; see also: <u>bioRxiv preprint</u>).

#### Journal Articles

MMWR: <u>Multistate Outbreak of SARS-CoV-2 B.1.1.529 (Omicron) Variant Infections Among</u>

<u>Persons in a Social Network Attending a Convention — New York City, November 18—December</u>

<u>20, 2021</u> (18 February 2022)

"What is already known about this topic? The SARS-CoV-2 Omicron variant is highly transmissible; is believed to have partial escape from infection- and vaccine-induced immunity; and is responsible for the recent rapid increase in U.S. cases.

What is added by this report? Attack rates among a cohort of persons attending a convention were high, but lower among infected attendees' household members. There were fewer infections among vaccinated attendees who had received a COVID-19 vaccine booster dose.

What are the implications for public health practice? Data from this investigation reinforce the importance of COVID-19 booster doses and early notification in combination with other multicomponent prevention measures to limit transmission and prevent severe illness from Omicron and other SARS-CoV-2 variants."

MMWR: <u>Genomic Surveillance for SARS-CoV-2 Variants: Predominance of the Delta (B.1.617.2)</u> and Omicron (B.1.1.529) Variants — United States, June 2021–January 2022 (11 February 2022)

"What is already known about this topic? CDC conducts genomic surveillance to track SARS-CoV-2 variants in the United States.

What is added by this report? CDC's SARS-CoV-2 genomic surveillance has been expanded to incorporate sequence data from public repositories and to produce weighted estimates of variant proportions at the jurisdiction level. The Delta (B.1.617.2 and AY sublineages) variant rose to predominance in late June 2021, followed by the rapid rise of Omicron (B.1.1.529 and BA sublineages) in December 2021.

What are the implications for public health practice? The dynamic landscape of SARS-CoV-2 variants in 2021, including Delta- and Omicron-driven resurgences of SARS-CoV-2

transmission across the United States, underscores the importance of robust genomic surveillance efforts to inform public health planning and practice."

Science: <u>Structures of the Omicron Spike trimer with ACE2 and an anti-Omicron antibody</u> (08 February 2022)

"The SARS-CoV-2 Omicron variant has become the dominant infective strain. We report the structures of the Omicron spike trimer on its own or in complex with ACE2 or an anti-Omicron antibody. Most Omicron mutations are located on the surface of the spike protein, which change binding epitopes to many current antibodies. In the ACE2 binding site, compensating mutations strengthen RBD binding to ACE2. Both the RBD and the apo form of the Omicron spike trimer are thermodynamically unstable. An unusual RBD-RBD interaction in the ACE2-spike complex supports the open conformation and further reinforces ACE2 binding to the spike trimer. A broad-spectrum therapeutic antibody, JMB2002, which has completed a Phase 1 clinical trial, maintains neutralizing activity against Omicron. JMB2002 binds to RBD differently from other characterized antibodies and inhibits ACE2 binding."

Am J Pathol: <u>Signals of significantly increased vaccine breakthrough, decreased hospitalization</u> rates, and less severe disease in patients with COVID-19 caused by the Omicron variant of SARS-COV-2 in Houston, Texas (03 February 2022)

"Genetic variants of SARS-CoV-2 continue to dramatically alter the landscape of the COVID-19 pandemic. The recently described variant of concern designated Omicron (B.1.1.529) has rapidly spread worldwide and is now responsible for the majority of COVID-19 cases in many countries. Because Omicron was recognized very recently, many knowledge gaps exist about its epidemiology, clinical severity, and disease course. A genome sequencing study of SARS-CoV-2 in the Houston Methodist healthcare system identified 4,468 symptomatic patients with infections caused by Omicron from late November 2021 through January 5, 2022. Omicron very rapidly increased in only three weeks to cause 90% of all new COVID-19 cases, and at the end of the study period caused 98% of new cases. Compared to patients infected with either Alpha or Delta variants in our healthcare system, Omicron patients were significantly younger, had significantly increased vaccine breakthrough rates, and were significantly less likely to be hospitalized. Omicron patients required less intense respiratory support and had a shorter length of hospital stay, consistent with on average decreased disease severity. Two patients with Omicron "stealth" sublineage BA.2 also were identified. The data document the unusually rapid spread and increased occurrence of COVID-19 caused by the Omicron variant in metropolitan Houston, and address the lack of information about disease character among US patients."

Front Med: <u>Genomic and Virological Characterization of SARS-CoV-2 Variants in a Subset of Unvaccinated and Vaccinated U.S. Military Personnel</u> (27 January 2022)

"The emergence of SARS-CoV-2 variants complicates efforts to control the COVID-19 pandemic. Increasing genomic surveillance of SARS-CoV-2 is imperative for early detection of emerging variants, to trace the movement of variants, and to monitor effectiveness of countermeasures. Additionally, determining the amount of viable virus present in clinical samples is helpful to better understand the impact these variants have on viral shedding. In this study, we analyzed nasal swab samples collected between March 2020 and early November 2021 from a cohort of United States (U.S.) military personnel and healthcare system beneficiaries stationed worldwide as a part of the Defense Health Agency's (DHA) Global Emerging Infections Surveillance (GEIS) program. SARS-CoV-2 quantitative real time reverse-transcription PCR (qRT-PCR) positive samples were characterized by nextgeneration sequencing and a subset was analyzed for isolation and quantification of viable virus. Not surprisingly, we found that the Delta variant is the predominant strain circulating among U.S. military personnel beginning in July 2021 and primarily represents cases of vaccine breakthrough infections (VBIs). Among VBIs, we found a 50-fold increase in viable virus in nasal swab samples from Delta variant cases when compared to cases involving other variants. Notably, we found a 40-fold increase in viable virus in nasal swab samples from VBIs involving Delta as compared to unvaccinated personnel infected with other variants prior to the availability of approved vaccines. This study provides important insight about the genomic and virological characterization of SARS-CoV-2 isolates from a unique study population with a global presence."

# Transmission, Exposure, and Testing

## News in Brief

"Americans are tired of the pandemic. But disease experts preach caution — and endure a 'kill the messenger' moment" ( $\underline{WP}$ ).

"How sneezing hamsters sparked a COVID outbreak in Hong Kong" (Nature; see also: preprint at SSRN).

"New York City might have rat COVID, but it's probably fine" (Curbed).

A Turkish man with leukemia set a new record by testing positive for COVID-19 for 14 straight months (Reuters).

# Journal Articles

MMWR: <u>Investigation of SARS-CoV-2 Transmission Associated With a Large Indoor Convention</u>
— <u>New York City, November–December 2021</u> (18 February 2022)

"What is already known about this topic? The SARS-CoV-2 Delta (B.1.617.2) and Omicron (B.1.1.529) variants are highly transmissible. Outbreaks have been reported among vaccinated populations in indoor settings where mask use was limited.

What is added by this report? Despite multiple introductions as evidenced by detection of at least three sublineages of SARS-CoV-2, this investigation did not find evidence of widespread transmission among a highly vaccinated population at a large event in an indoor setting where mask use was required and monitored.

What are the implications for public health practice? Implementing multiple prevention measures (vaccinations and boosters, consistent mask wearing, enhanced indoor ventilation, and testing after text notification) can limit the transmission of SARS-CoV-2 at large events, including highly transmissible variants."

MMWR: <u>Effectiveness of Face Mask or Respirator Use in Indoor Public Settings for Prevention of SARS-CoV-2 Infection — California, February—December 2021</u> (11 February 2022)

"What is already known about this topic? Face masks or respirators (N95/KN95s) effectively filter virus-sized particles in laboratory settings. The real-world effectiveness of face coverings to prevent acquisition of SARS-CoV-2 infection has not been widely studied.

What is added by this report? Consistent use of a face mask or respirator in indoor public settings was associated with lower odds of a positive SARS-CoV-2 test result (adjusted odds ratio = 0.44). Use of respirators with higher filtration capacity was associated with the most protection, compared with no mask use.

What are the implications for public health practice? In addition to being up to date with recommended COVID-19 vaccinations, consistently wearing a comfortable, well-fitting face mask or respirator in indoor public settings protects against acquisition of SARS-CoV-2 infection; a respirator offers the best protection."

Clin Infect Dis: <u>Rapid control of hospital-based SARS-CoV-2 Omicron clusters through daily testing and universal use of N95 respirators</u> (07 February 2022)

"The highly contagious SARS-CoV-2 Omicron variant increases risk for nosocomial transmission despite universal masking, admission testing, and symptom screening. We report large increases in hospital-onset infections and 2 unit-based clusters. The clusters rapidly abated after instituting universal N95 respirators and daily testing. Broader use of these strategies may prevent nosocomial transmissions."

Aerosp Med Hum Perform: <u>Air Evacuation of Citizens During the COVID-19 Epidemic</u> (01 February 2022)

"BACKGROUND: The coronavirus epidemic originated in China, having its epicenter in Wuhan. This was the first place in the world to adopt social distancing measures to contain the disease on January 23rd, 2020. After the initial isolation, several countries started making diplomatic plans to evacuate and repatriate their citizens, with the permission of the Chinese authorities. Due to the high risk of exposure of the transported passengers, evacuations were conducted with preventive measures against contamination by biological agents.

CASE REPORT: We report the air evacuation of 39 passengers from China to Brazil. Five passengers were transported to Poland and the remaining 34 went to Brazil, where they remained in quarantine for 14 d. The mission was triggered on February 4th, named 'Operation Return to Brazil', and conducted by military personnel of the Brazilian Air Force. The mission was accomplished in 6 days; the flight from Wuhan lasted 25 h 20 min; and, additionally, there were on-ground preparations.

DISCUSSION: Only with adequate isolation and protective measures was it possible to air evacuate the potentially contaminated passengers in the initial phase of the pandemic. Specific protective equipment (Personal Protective Equipment – PPE) is mandatory for missions in which the properties of the potentially contagious biological agent are not fully known, as was the case. Due to the risk of contamination of passengers and the likely evolution of the transport into an aeromedical evacuation, protocols stating the minimum safety conditions for this kind of patient transport must be followed, with consideration for the patient as well as the crew."

FEMS Microbes: <u>Predicting daily COVID-19 case rates from SARS-CoV-2 RNA concentrations across a diversity of wastewater catchments</u> (10 January 2022)

"We assessed the relationship between municipality COVID-19 case rates and SARS-CoV-2 concentrations in the primary sludge of corresponding wastewater treatment facilities. Over 1700 daily primary sludge samples were collected from six wastewater treatment facilities with catchments serving 18 cities and towns in Connecticut, USA. Samples were analyzed for SARS-CoV-2 RNA concentrations during a 10 month time period that overlapped with October 2020 and winter/spring 2021 COVID-19 outbreaks in each municipality. We fit lagged regression models to estimate reported case rates in the six municipalities from SARS-CoV-2 RNA concentrations collected daily from corresponding wastewater treatment facilities. Results demonstrate the ability of SARS-CoV-2 RNA concentrations in primary sludge to estimate COVID-19 reported case rates across treatment facilities and wastewater catchments, with coverage probabilities ranging from 0.94 to 0.96. Lags of 0 to 1 days resulted in the greatest predictive power for the model. Leave-one-out cross validation

suggests that the model can be broadly applied to wastewater catchments that range in more than one order of magnitude in population served. The close relationship between case rates and SARS-CoV-2 concentrations demonstrates the utility of using primary sludge samples for monitoring COVID-19 outbreak dynamics. Estimating case rates from wastewater data can be useful in locations with limited testing availability, testing disparities, or delays in individual COVID-19 testing programs."

## **COVID-19 Vaccines**

# News in Brief

"Study suggests Omicron-specific booster may not provide more protection" (<u>STAT</u>; see also: <u>bioRxiv preprint</u>).

"Why Covid-19 vaccines are a freaking miracle" (STAT).

"Vaccine scientists have been chasing variants. Now, they're seeking a universal coronavirus vaccine" (WP).

"Mix 'n' match COVID-19 vaccine boosting may lower breakthrough cases" (<u>CIDRAP</u>; see also: NEJM Letter to the Editor).

"Why were scientists so slow to study Covid-19 vaccines and menstruation?" (Vox)

#### **Journal Articles**

MMWR: Waning 2-Dose and 3-Dose Effectiveness of mRNA Vaccines Against COVID-19—
Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among
Adults During Periods of Delta and Omicron Variant Predominance — VISION Network, 10
States, August 2021—January 2022 (18 February 2022)

"What is already known about this topic? Protection against COVID-19 after 2 doses of mRNA vaccine wanes, but little is known about durability of protection after 3 doses.

What is added by this report? Vaccine effectiveness (VE) against COVID-19—associated emergency department/urgent care (ED/UC) visits and hospitalizations was higher after the third dose than after the second dose but waned with time since vaccination. During the Omicron-predominant period, VE against COVID-19—associated ED/UC visits and hospitalizations was 87% and 91%, respectively, during the 2 months after a third dose and decreased to 66% and 78% by the fourth month after a third dose. Protection against hospitalizations exceeded that against ED/UC visits.

What are the implications for public health practice? All eligible persons should remain up to date with recommended COVID-19 vaccinations to best protect against COVID-19—associated hospitalizations and ED/UC visits."

MMWR: <u>Safety Monitoring of COVID-19 Vaccine Booster Doses Among Adults — United States,</u> <u>September 22, 2021–February 6, 2022</u> (18 February 2022)

"What is already known about this topic? In preauthorization trials, adverse reactions were reported less frequently following a homologous COVID-19 mRNA vaccine booster dose than after receipt of the second primary dose.

What is added by this report? Review of surveillance data found that local and systemic reactions were less frequent after a homologous COVID-19 mRNA vaccine booster dose than after the second primary vaccine dose. Myocarditis was rarely reported following an mRNA vaccine booster dose.

What are the implications for public health practice? All persons aged ≥12 years should receive a COVID-19 booster dose. Vaccination providers should educate patients that local and systemic reactions are expected following a homologous COVID-19 mRNA vaccine booster; however, these reactions are less common than those following the second primary series dose."

Radiology: <u>Myocardial Injury Pattern at MRI in COVID-19 Vaccine-associated Myocarditis.</u>
<u>Radiology</u> (15 February 2022)

"Background: There is limited data on the pattern and severity of myocardial injury in patients with COVID-19 vaccination associated myocarditis.

Methods: In this retrospective cohort study, consecutive adult patients with myocarditis with at least one T1-based and at least one T2-based abnormality on cardiac MRI performed at a tertiary referral hospital between 2019-2021 were included. Patients were classified into one of three groups: myocarditis following COVID-19 vaccination, myocarditis following COVID-19 illness, and other myocarditis not associated COVID-19 vaccination or illness.

Results: Of the 92 included patients, 21 (22%) had myocarditis following COVID-19 vaccination (mean age 31 years ±14 [standard deviation]; 17 men; mRNA-1273 in 12 [57%] and BNT162b2 in 9 [43%]). Ten patients (11%) had myocarditis following COVID-19 illness (mean age 51 years ±14; 3 men), and 61 (66%) had other myocarditis (mean age 44 years ±18; 36 men). MRI findings in vaccine associated myocarditis included late gadolinium enhancement (LGE) in 17 (81%) and left ventricular dysfunction in 6 (29%). Compared with other causes of myocarditis, patients with vaccine associated myocarditis had higher left ventricular ejection fraction and less extensive LGE, even after controlling for age, sex, and duration between symptom onset and MRI. The most frequent location of LGE in all groups was subepicardial at the basal inferolateral wall, although septal involvement was less

common in vaccine associated myocarditis. At short-term follow-up (median 22 [IQR 7-48] days), all patients with vaccine associated myocarditis were asymptomatic with no adverse events.

Conclusions: Cardiac MRI demonstrated a similar pattern of myocardial injury in vaccine associated myocarditis compared to other causes, although abnormalities were less severe, with less frequent septal involvement, and no adverse events over short-term follow-up."

Emerg Infect Dis: <u>Multisystem Inflammatory Syndrome in Adult after First Dose of mRNA Vaccine</u> (11 February 2022)

"A 32-year-old man in Japan experienced respiratory failure after receiving the first dose of coronavirus disease (COVID-19) vaccine. He was treated with noninvasive ventilation and corticosteroids. Serologic test results suggested previous COVID-19; therefore, he received a diagnosis of multisystem inflammatory syndrome. COVID-19 vaccination could be a trigger for this condition."

Clin Infect Dis: <u>Comparative Effectiveness of COVID-19 Vaccines against the Delta Variant</u> (07 February 2022)

"Background: There is a lack of data regarding how the delta variant of coronavirus disease 2019 (COVID-19) has impacted the effectiveness of the BNT162b2 (Pfizer-BioNTech), mRNA-1273 (Moderna), and Ad26.COV2.S (Johnson & Johnson-Janssen) vaccines at preventing SARS-CoV-2 infection and COVID-19 hospitalization.

Methods: We compared the effectiveness of the three vaccines during the pre- and postdelta variant period (before and after July 1 st, 2021) in a large cohort of vaccinated and unvaccinated patients in the Michigan Medicine healthcare system. We assessed vaccine effectiveness using two analyses: an Inverse Propensity Weighted (IPW) Kaplan-Meier (KM) analysis based on time from vaccination, and a Cox model based on calendar time with vaccination as a time-varying covariate.

Results: Compared to Ad26.COV2.S recipients, the risk of hospitalization for COVID-19 in the post-delta variant period was lower for BNT162b2 recipients (HR=0.37; 95% CI: [0.14-0.98]; p=0.05) and mRNA-1273 recipients (HR=0.21; 95% CI: [0.07-0.64]; p=0.006). Recipients of the mRNA-1273 vaccine had a lower risk of SARS-CoV-2 infection than Ad26.COV2.S recipients (HR=0.6; 95% CI: [0.43-0.83]; p=0.003) and BNT162b2 recipients (HR=0.64; 95% CI: [0.54-0.76]; p<0.001). After July 1st, efficacy against SARS-CoV-2 infection declined for Ad26.COV2.S recipients (VE=76% before; VE=49% after; p=0.02), BNT162b2 recipients (VE=87% before; VE=52% after; p<0.001), and mRNA-1273 recipients (VE=92% before; VE=70% after; p<0.001). Waning immunity and the delta variant contributed independently and significantly to this decline.

Discussion: Although there is a substantial decline in effectiveness, the approved COVID-19 vaccines remain effective against infection and hospitalization due to the delta variant. The mRNA-based vaccines are more effective than the Ad26.COV2.S vaccine."

# **Breakthrough Infections and Reinfections**

# News in Brief

"COVID reinfections surge during Omicron onslaught" (<u>Nature</u>; see also: <u>NEJM Letter to the</u> Editor and medRxiv preprint).

#### Journal Articles

Int J Infect Dis: <u>Hospitalized patients with breakthrough COVID-19</u>: <u>Clinical features and poor outcome predictors</u> (13 February 2022)

"Objectives: To describe breakthrough COVID-19 in patients who needed hospitalization and the factors associated with poor outcomes.

Methods: A retrospective study on complete (diagnosed two weeks after the second dose of the Pfizer/Moderna/AstraZeneca or first dose of the Janssen vaccine was administered) or partial vaccine scheme (CV or PV) patients hospitalized for COVID-19 between December 27, 2020, and October 17, 2021, was conducted. The main outcomes were all-cause mortality and the need for invasive mechanical ventilation (IMV). The baseline factors associated with the outcomes were analyzed by multiple logistic regression, estimating the odds ratios (OR; 95% CI).

Results: One hundred and forty-five patients (101 CV) were included. The CV subgroup was mainly composed of elderly males with high comorbidity (Charlson index  $\geq$ 3, 72%; immunosuppression, 20%), with bilateral pneumonia in 63.4%; limited therapeutic effort (LTE) was agreed upon for 28% of the patients. In the CV subgroup, endotracheal intubation was required in 10.9%, reaching 15.3% when excluding LTE patients; the global mortality was 22.8% and 41.4% in the subgroup with LTE. Although the PV patients were younger and had fewer comorbidities, the main outcomes did not differ significantly between the CV and PV groups. The predictors of poor outcomes were age  $\geq$  65 years, confusion, ferritin > 500 mg/L, extensive lung infiltrates, and a Charlson index  $\geq$  3.

Conclusions: Fully vaccinated patients hospitalized due to breakthrough COVID-19 tend to be elderly, with comorbidities, and have high mortality."

## **Treatments and Management**

# News in Brief

Gilead said its antiviral COVID treatment remdesivir retains activity against Omicron and likely its subvariant, BA.2 (Gilead).

"Why remdesivir, a highly effective COVID treatment, is a last resort for providers" (NPR).

"Eagerly awaited COVID lifesavers molnupiravir, Paxlovid now wait for patients" (CIDRAP).

"What a bottle of ivermectin reveals about the shadowy world of COVID telemedicine" (NPR).

"Arkansas jail's ivermectin experiments recall historical medical abuse of imprisoned minorities" (Guardian).

## **Journal Articles**

NEJM: Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19 (16 February 2022)

"Background: Nirmatrelvir is an orally administered severe acute respiratory syndrome coronavirus 2 main protease (Mpro) inhibitor with potent pan-human-coronavirus activity in vitro.

Methods: We conducted a phase 2-3 double-blind, randomized, controlled trial in which symptomatic, unvaccinated, nonhospitalized adults at high risk for progression to severe coronavirus disease 2019 (Covid-19) were assigned in a 1:1 ratio to receive either 300 mg of nirmatrelvir plus 100 mg of ritonavir (a pharmacokinetic enhancer) or placebo every 12 hours for 5 days. Covid-19-related hospitalization or death from any cause through day 28, viral load, and safety were evaluated.

Results: A total of 2246 patients underwent randomization; 1120 patients received nirmatrelvir plus ritonavir (nirmatrelvir group) and 1126 received placebo (placebo group). In the planned interim analysis of patients treated within 3 days after symptom onset (modified intention-to treat population, comprising 774 of the 1361 patients in the full analysis population), the incidence of Covid-19-related hospitalization or death by day 28 was lower in the nirmatrelvir group than in the placebo group by 6.32 percentage points (95% confidence interval [CI], -9.04 to -3.59; P<0.001; relative risk reduction, 89.1%); the incidence was 0.77% (3 of 389 patients) in the nirmatrelvir group, with 0 deaths, as compared with 7.01% (27 of 385 patients) in the placebo group, with 7 deaths. Efficacy was maintained in the final analysis involving the 1379 patients in the modified intention-to-treat population, with a difference of -5.81 percentage points (95% CI, -7.78 to -3.84; P<0.001; relative risk reduction, 88.9%). All 13 deaths occurred in the placebo group. The viral load was lower with nirmaltrelvir plus ritonavir than with placebo at day 5 of

treatment, with an adjusted mean difference of -0.868 log10 copies per milliliter when treatment was initiated within 3 days after the onset of symptoms. The incidence of adverse events that emerged during the treatment period was similar in the two groups (any adverse event, 22.6% with nirmatrelvir plus ritonavir vs. 23.9% with placebo; serious adverse events, 1.6% vs. 6.6%; and adverse events leading to discontinuation of the drugs or placebo, 2.1% vs. 4.2%). Dysgeusia (5.6% vs. 0.3%) and diarrhea (3.1% vs. 1.6%) occurred more frequently with nirmatrelvir plus ritonavir than with placebo.

Conclusions: Treatment of symptomatic Covid-19 with nirmatrelvir plus ritonavir resulted in a risk of progression to severe Covid-19 that was 89% lower than the risk with placebo, without evident safety concerns."

Lancet: <u>Casirivimab and imdevimab in patients admitted to hospital with COVID-19</u> (<u>RECOVERY</u>): a randomised, controlled, open-label, platform trial (12 February 2022)

"Background: Casirivimab and imdevimab are non-competing monoclonal antibodies that bind to two different sites on the receptor binding domain of the SARS-CoV-2 spike glycoprotein, blocking viral entry into host cells. We aimed to evaluate the efficacy and safety of casirivimab and imdevimab administered in combination in patients admitted to hospital with COVID-19.

Methods: RECOVERY is a randomised, controlled, open-label platform trial comparing several possible treatments with usual care in patients admitted to hospital with COVID-19. 127 UK hospitals took part in the evaluation of casirivimab and imdevimab. Eligible participants were any patients aged at least 12 years admitted to hospital with clinically suspected or laboratory-confirmed SARS-CoV-2 infection. Participants were randomly assigned (1:1) to either usual standard of care alone or usual care plus casirivimab 4 g and imdevimab 4 g administered together in a single intravenous infusion. Investigators and data assessors were masked to analyses of the outcome data during the trial. The primary outcome was 28-day all-cause mortality assessed by intention to treat, first only in patients without detectable antibodies to SARS-CoV-2 infection at randomisation (ie, those who were seronegative) and then in the overall population. Safety was assessed in all participants who received casirivimab and imdevimab. The trial is registered with ISRCTN (50189673) and ClinicalTrials.gov (NCT04381936).

Findings: Between Sept 18, 2020, and May 22, 2021, 9785 patients enrolled in RECOVERY were eligible for casirivimab and imdevimab, of which 4839 were randomly assigned to casirivimab and imdevimab plus usual care and 4946 to usual care alone. 3153 (32%) of 9785 patients were seronegative, 5272 (54%) were seropositive, and 1360 (14%) had unknown baseline antibody status. 812 (8%) patients were known to have received at least one dose of a SARS-CoV-2 vaccine. In the primary efficacy population of seronegative patients, 396 (24%) of 1633 patients allocated to casirivimab and imdevimab versus 452

(30%) of 1520 patients allocated to usual care died within 28 days (rate ratio [RR] 0·79, 95% CI 0·69-0·91; p=0·0009). In an analysis of all randomly assigned patients (regardless of baseline antibody status), 943 (19%) of 4839 patients allocated to casirivimab and imdevimab versus 1029 (21%) of 4946 patients allocated to usual care died within 28 days (RR 0·94, 95% CI 0·86-1·02; p=0·14). The proportional effect of casirivimab and imdevimab on mortality differed significantly between seropositive and seronegative patients (p value for heterogeneity=0·002). There were no deaths attributed to the treatment, or meaningful between-group differences in the pre-specified safety outcomes of cause-specific mortality, cardiac arrhythmia, thrombosis, or major bleeding events. Serious adverse reactions reported in seven (<1%) participants were believed by the local investigator to be related to treatment with casirivimab and imdevimab.

Interpretation: In patients admitted to hospital with COVID-19, the monoclonal antibody combination of casirivimab and imdevimab reduced 28-day mortality in patients who were seronegative (and therefore had not mounted their own humoral immune response) at baseline but not in those who were seropositive at baseline."

MMWR: <u>Clinical Characteristics and Outcomes Among Adults Hospitalized with Laboratory-Confirmed SARS-CoV-2 Infection During Periods of B.1.617.2 (Delta) and B.1.1.529 (Omicron) Variant Predominance — One Hospital, California, July 15—September 23, 2021, and December 21, 2021—January 27, 2022 (11 February 2022)</u>

"What is already known about this topic? The SARS-CoV-2 Omicron variant became predominant in the United States in mid-December 2021, coinciding with a rise in SARS-CoV-2—associated hospitalizations.

What is added by this report? Among adults hospitalized with SARS-CoV-2 infection during Omicron predominance, COVID-19 vaccination, including with a booster dose, was associated with lower likelihood of intensive care unit admission. Compared with patients during the period of Delta predominance, Omicron-period patients had less severe illness, largely driven by an increased proportion who were fully vaccinated. Approximately 20% of early Omicron-period hospitalizations were for non–COVID-19 conditions, particularly among young and vaccinated adults.

What are the implications for public health practice? COVID-19 vaccination, particularly a booster dose, continues to be critical in mitigating the health care burden of the Omicron variant."

Clin Infect Dis: <u>Comparing Covid-19 pandemic waves in hospitalized patients – a retrospective,</u> multicenter, cohort study (10 February 2022)

"Background: Covid-19 disease was first diagnosed in Israel at the end of February 2020. Until the end of June 2021 842,536 confirmed cases and 6428 deaths were accumulated.

The aim of our multicenter retrospective cohort study is to describe the demographic and clinical characteristics of hospitalized patients and to compare the pandemic waves before immunization.

Methods: Out of 22302 patients hospitalized in general medical centers we randomly selected 6329 admissions for the study. Of these, 3582 and 1106 were eligible for the study in the first period (1 st & 2 nd waves), and in the second period (3 rd wave), respectively.

Results: Thirty-day mortality was higher in the 2nd period than in the 1st period, 25.20% versus 13.68% (P<0.001). Invasive mechanical ventilation supported 9.19% and 14.21% of the patients in the 1st period and 2nd period, respectively. Extracorporeal Membrane Oxygenation (ECMO) was used more than twice as often on the 2nd period.

Conclusions: Invasive ventilation, use of ECMO and mortality rate were 1.5 to 2 times higher on the 2 nd period than in the 1 st period. Patients of the 2 nd period had a more severe presentation and higher mortality than those of the 1 st period."

JAMA Netw Open: Efficacy of Niclosamide vs Placebo in SARS-CoV-2 Respiratory Viral Clearance, Viral Shedding, and Duration of Symptoms Among Patients With Mild to Moderate COVID-19: A Phase 2 Randomized Clinical Trial (09 February 2022)

"Question: Does oral niclosamide decrease the contagious period as determined by SARS-CoV-2 shedding among patients with mild to moderate COVID-19?

Findings: In this randomized clinical trial that included 73 adults with mild to moderate COVID-19, the proportion of participants achieving oropharyngeal clearance of SARS-CoV-2 at 3 days postenrollment was not statistically significantly different between patients given placebo and those given niclosamide. Niclosamide was well-tolerated.

Meaning: This study did not find a significant effect of niclosamide on decreasing the contagious period of SAR-CoV-2 infection."

JAMA Netw Open: <u>Prevalence of Select New Symptoms and Conditions Among Persons Aged Younger Than 20 Years and 20 Years or Older at 31 to 150 Days After Testing Positive or Negative for SARS-CoV-2</u> (04 February 2022)

"Question: Are select new symptoms and conditions more common among persons aged younger than 20 years and 20 years or older who tested positive for SARS-CoV-2 compared with those who tested negative?

Findings: In this cohort study of 338 024 persons younger than 20 years and 1 790 886 persons 20 years or older who were tested for SARS-CoV-2, new diagnoses of shortness of breath, nonspecific heart rate abnormalities, and type 2 diabetes were more common among those hospitalized after positive compared with negative test results; fatigue was more common among those aged 20 years or older.

Meaning: Given these findings, health care professionals should be aware of new symptoms and conditions that may develop after SARS-CoV-2 infection, particularly among those hospitalized."

# **Pre-Existing Conditions and Comorbidities**

# News in Brief

"A disabled activist speaks out about feeling 'disposable'" (KHN).

"Most vulnerable still in jeopardy as COVID precautions ease" (AP).

"The millions of people stuck in pandemic limbo — what does society owe immunocompromised people?" (Atlantic)

### **Journal Articles**

BMJ Open: <u>Association between pharmaceutical modulation of oestrogen in postmenopausal</u> <u>women in Sweden and death due to COVID-19: a cohort study</u> (14 February 2022)

"Objective: Determine whether augmentation of oestrogen in postmenopausal women decreases the risk of death following COVID-19.

Design: Nationwide registry-based study in Sweden based on registries from the Swedish Public Health Agency (all individuals who tested positive for SARS-CoV-2); Statistics Sweden (socioeconomical variables) and the National Board of Health and Welfare (causes of death). Participants: Postmenopausal women between 50 and 80 years of age with verified COVID-19.

Interventions: Pharmaceutical modulation of oestrogen as defined by (1) women with previously diagnosed breast cancer and receiving endocrine therapy (decreased systemic oestrogen levels); (2) women receiving hormone replacement therapy (increased systemic oestrogen levels) and (3) a control group not fulfilling requirements for group 1 or 2 (postmenopausal oestrogen levels). Adjustments were made for potential confounders such as age, annual disposable income (richest group as the reference category), highest level of education (primary, secondary and tertiary (reference)) and the weighted Charlson Comorbidity Index (wCCI). Primary outcome measure: Death following COVID-19.

Results: From a nationwide cohort consisting of 49 853 women diagnosed with COVID-19 between 4 February and 14 September 2020 in Sweden, 16 693 were between 50 and 80 years of age. We included 14 685 women in the study with 11 923 (81%) in the control

group, 227 (2%) women in group 1 and 2535 (17%) women in group 2. The unadjusted ORs for death following COVID-19 were 2.35 (95% CI 1.51 to 3.65) for group 1 and 0.45 (0.34 to 0.6) for group 2. Only the adjusted OR for death remained significant for group 2 with OR 0.47 (0.34 to 0.63). Absolute risk of death was 4.6% for the control group vs 10.1% and 2.1%, for the decreased and increased oestrogen groups, respectively. The risk of death due to COVID-19 was significantly associated with: age, OR 1.15 (1.14 to 1.17); annual income, poorest 2.79 (1.96 to 3.97), poor 2.43 (91.71 to 3.46) and middle 1.64 (1.11 to 2.41); and education (primary 1.4 (1.07 to 1.81)) and wCCI 1.13 (1.1 to 1.16).

Conclusions: Oestrogen supplementation in postmenopausal women is associated with a decreased risk of dying from COVID-19 in this nationwide cohort study. These findings are limited by the retrospective and non-randomised design. Further randomised intervention trials are warranted."

Clin Infect Dis: Real-world Effectiveness of the SARS-CoV-2 mRNA Vaccines in Preventing Confirmed Infection in Patients on Chronic Hemodialysis (09 February 2022)

"Background: Persons on chronic hemodialysis have a significantly diminished humoral immune response to SARS-CoV-2 vaccines. Whether this translates to reduced vaccine effectiveness (VE) is unknown.

Methods: We used the US Department of Veterans Affairs COVID-19 Shared Data Resource to identify all Veterans who were tested for SARS-CoV-2 between January 26, 2021 and August 31, 2021. Using International Classification of Diseases, 10 th edition codes and attendance at a dialysis clinic or center, we identified those who were on chronic hemodialysis. We used a test-negative, case-control design using a doubly-robust logistic regression model to determine the VE of the BNT-162b2 (Pfizer) or mRNA-1273 (Moderna) vaccines in preventing confirmed SARS-CoV-2 infection.

Results: Among 847,199 Veterans tested for SARS-CoV-2 between January 26, 2021 and August 31, 2021, there were 6,076 Veterans on chronic hemodialysis. Among those, we identified 1,270 cases (580 fully vaccinated) and 2,959 controls (2,120 fully vaccinated). The overall VE >14 days after the second dose in preventing documented infection was 68.2% (95% CI:62.6,72.9). VE was 68.9% (95% CI:61.9,74.7) for Pfizer-BNT-162b2 and 66.7% (95% CI:58.9,73.0) for Moderna-mRNA-1273 vaccine. There was no difference in VE by age (<70 vs. >70 years), race or sex. There were no events recorded in persons with a Charlson's comorbidity index score of <2.

Conclusion: VE of two doses of current mRNA vaccines in preventing SARS-CoV-2 infection in persons on chronic hemodialysis is lower than historic VE rates in the general population. Effect of additional doses in improving VE in this special population needs further study."

# **Long COVID and Other Complications**

# News in Brief

"Long COVID less likely in the vaccinated — even getting vaccinated after infection appears to help, review concludes" (Medpage; see also: rapid evidence briefing document from UK Health Security Agency).

"Scientists propose cause of symptoms, treatment for long COVID-19" (CIDRAP).

"Even as omicron infections trend down, long COVID remains a threat to the military" (BAS).

"'Good, not great': Some long Covid patients see their symptoms improve, but full recovery is elusive" (<u>STAT</u>).

"COVID long haulers are calling attention to chronic illnesses — but society is not prepared for the growing crisis of long COVID" (SciAm).

"Pandemics disable people — the history lesson that policymakers ignore" (Nature).

## **Journal Articles**

#### Guidelines

Clin Microbiol Infect: ESCMID rapid guidelines for assessment and management of long COVID (16 February 2022)

"Scope: The aim of these guidelines is to provide evidence-based recommendations for assessment and management of individuals with persistent symptoms after acute COVID-19 infection, and provide a definition for this entity, termed "long COVID".

Methods: We performed a search of the literature on studies addressing epidemiology, symptoms, assessment, and treatment of long COVID. The recommendations were grouped by these headings and by organ systems for assessment and treatment. An expert opinion definition of long COVID is provided. Symptoms were reviewed by a search of the available literature. For assessment recommendations, we aimed to perform a diagnostic meta-analysis, but no studies provided relevant results. For treatment recommendations we performed a systematic review of the literature in accordance with the PRISMA statement. We aimed to evaluate patient-related outcomes, including quality of life, return to baseline physical activity, and return to work. Quality assessment of studies included in the systematic review is provided according to study design.

Recommendations: Evidence was insufficient to provide any recommendation other than conditional guidance. The panel recommends considering routine blood tests, chest imaging and pulmonary functions tests for patients with persistent respiratory symptoms at 3

months. Other tests should be performed mainly to exclude other conditions according to symptoms. For management, no evidence-based recommendations could be provided. Physical and respiratory rehabilitation should be considered. On the basis of limited evidence, the panel suggests designing high quality prospective clinical studies/trials, including a control group, to further evaluate assessment and management of individuals with persistent symptoms of COVID-19."

#### Other Literature

JAMA Ophthalmol: <u>COVID-19-Related Chronic Bilateral Dacryoadenitis: A Clinicopathological</u> Study (17 February 2022)

"Question: Is SARS-CoV-2 associated with lacrimal gland tissue and dacryoadenitis?

Findings: In this case-control study of 2 Japanese women, histopathologic analysis of surgically excised lacrimal gland tissues from the patient with COVID-19 showed characteristic glandular damage and polymorphonuclear leukocyte infiltration within the epithelium, together with marked inflammation made up of lymphocytes and plasma cells surrounding the glands. Immunoreactivity for nucleocapsid protein of SARS-CoV-2 as well as angiotensin-converting enzyme 2 was noted in the lacrimal gland tissue.

Meaning: These findings suggest that SARS-CoV-2 may target lacrimal gland tissue and manifest as chronic inflammation."

Arthritis Rheumatol: Endothelial cell-activating antibodies in COVID-19 (17 February 2022)

"Objective: While endothelial dysfunction has been implicated in the widespread thrombo-inflammatory complications of coronavirus disease-19 (COVID-19), the upstream mediators of endotheliopathy remain for the most part cryptic. Our aim was to identify circulating factors contributing to endothelial cell activation and dysfunction in COVID-19.

Methods: Human endothelial cells were cultured in the presence of serum or plasma from 244 patients hospitalized with COVID-19 and plasma from 100 patients with non-COVID sepsis. Cell adhesion molecules (E-selectin, VCAM-1, and ICAM-1) were quantified by in-cell ELISA.

Results: Serum and plasma from patients with COVID-19 increased surface expression of cell adhesion molecules. Furthermore, levels of soluble ICAM-1 and E-selectin were elevated in patient serum and tracked with disease severity. The presence of circulating antiphospholipid antibodies was a strong marker of the ability of COVID-19 serum to activate endothelium. Depletion of total IgG from antiphospholipid antibody-positive serum markedly restrained upregulation of cell adhesion molecules. Conversely, supplementation of control serum with patient IgG was sufficient to trigger endothelial activation.

Conclusion: These data are the first to suggest that some patients with COVID-19 have potentially diverse antibodies that drive endotheliopathy, adding important context regarding thrombo-inflammatory effects of autoantibodies in severe COVID-19."

BMJ: Risk of persistent and new clinical sequelae among adults aged 65 years and older during the post-acute phase of SARS-CoV-2 infection: retrospective cohort study (09 February 2022)

"Objective: To characterize the risk of persistent and new clinical sequelae in adults aged ≥65 years after the acute phase of SARS-CoV-2 infection.

Participants: Individuals aged ≥65 years who were continuously enrolled in a Medicare Advantage plan with coverage of prescription drugs from January 2019 to the date of diagnosis of SARS-CoV-2 infection, matched by propensity score to three comparison groups that did not have covid-19: 2020 comparison group (n=87 337), historical 2019 comparison group (n=88 070), and historical comparison group with viral lower respiratory tract illness (n=73 490).

Main outcome measures: The presence of persistent and new sequelae at 21 or more days after a diagnosis of covid-19 was determined with ICD-10 (international classification of diseases, 10th revision) codes. Excess risk for sequelae caused by infection with SARS-CoV-2 was estimated for the 120 days after the acute phase of the illness with risk difference and hazard ratios, calculated with 95% Bonferroni corrected confidence intervals. The incidence of sequelae after the acute infection was analyzed by age, race, sex, and whether patients were admitted to hospital for covid-19.

Results: Among individuals who were diagnosed with SARS-CoV-2, 32% (27 698 of 87 337) sought medical attention in the post-acute period for one or more new or persistent clinical sequelae, which was 11% higher than the 2020 comparison group. Respiratory failure (risk difference 7.55, 95% confidence interval 7.18 to 8.01), fatigue (5.66, 5.03 to 6.27), hypertension (4.43, 2.27 to 6.37), memory difficulties (2.63, 2.23 to 3.13), kidney injury (2.59, 2.03 to 3.12), mental health diagnoses (2.50, 2.04 to 3.04), hypercoagulability 1.47 (1.2 to 1.73), and cardiac rhythm disorders (2.19, 1.76 to 2.57) had the greatest risk differences compared with the 2020 comparison group, with similar findings to the 2019 comparison group. Compared with the group with viral lower respiratory tract illness, however, only respiratory failure, dementia, and post-viral fatigue had increased risk differences of 2.39 (95% confidence interval 1.79 to 2.94), 0.71 (0.3 to 1.08), and 0.18 (0.11 to 0.26) per 100 patients, respectively. Individuals with severe covid-19 disease requiring admission to hospital had a markedly increased risk for most but not all clinical sequelae.

Conclusions: The results confirm an excess risk for persistent and new sequelae in adults aged ≥65 years after acute infection with SARS-CoV-2. Other than respiratory failure, dementia, and post-viral fatigue, the sequelae resembled those of viral lower respiratory

tract illness in older adults. These findings further highlight the wide range of important sequelae after acute infection with the SARS-CoV-2 virus."

Nat Med: Long-term cardiovascular outcomes of COVID-19 (07 February 2022)

"The cardiovascular complications of acute coronavirus disease 2019 (COVID-19) are well described, but the post-acute cardiovascular manifestations of COVID-19 have not yet been comprehensively characterized. Here we used national healthcare databases from the US Department of Veterans Affairs to build a cohort of 153,760 individuals with COVID-19, as well as two sets of control cohorts with 5,637,647 (contemporary controls) and 5,859,411 (historical controls) individuals, to estimate risks and 1-year burdens of a set of prespecified incident cardiovascular outcomes. We show that, beyond the first 30 d after infection, individuals with COVID-19 are at increased risk of incident cardiovascular disease spanning several categories, including cerebrovascular disorders, dysrhythmias, ischemic and non-ischemic heart disease, pericarditis, myocarditis, heart failure and thromboembolic disease. These risks and burdens were evident even among individuals who were not hospitalized during the acute phase of the infection and increased in a graded fashion according to the care setting during the acute phase (non-hospitalized, hospitalized and admitted to intensive care). Our results provide evidence that the risk and 1-year burden of cardiovascular disease in survivors of acute COVID-19 are substantial. Care pathways of those surviving the acute episode of COVID-19 should include attention to cardiovascular health and disease."

## **Pregnancy and Postpartum Period**

# News in Brief

"Global study launched to evaluate effects of COVID-19 variants and vaccination in pregnancy" (Oxford).

"Omicron revived a heartbreaking pandemic measure in NICUs" (Atlantic).

#### **Journal Articles**

MMWR: Effectiveness of Maternal Vaccination with mRNA COVID-19 Vaccine During Pregnancy Against COVID-19—Associated Hospitalization in Infants Aged <6 Months — 17 States, July 2021—January 2022 (18 February 2022)

"What is already known about this topic? COVID-19 vaccination during pregnancy is recommended to prevent severe illness and death in pregnant women. Infants are at risk

for COVID-19—associated complications, including respiratory failure and other life-threatening complications.

What is added by this report? Effectiveness of maternal completion of a 2-dose primary mRNA COVID-19 vaccination series during pregnancy against COVID-19 hospitalization among infants aged <6 months was 61% (95% CI = 31% to 78%). Effectiveness of completion of the primary COVID-19 vaccine series early and later in pregnancy was 32% (95% CI = -43% to 68%) and 80% (95% CI = -55% to 91%), respectively.

What are the implications for public health practice? Completion of a 2-dose mRNA COVID-19 vaccination series during pregnancy might help prevent COVID-19 hospitalization among infants aged <6 months."

JAMA: <u>Association of SARS-CoV-2 Infection With Serious Maternal Morbidity and Mortality</u> <u>From Obstetric Complications</u> (07 February 2022)

"Question: Among pregnant and postpartum individuals, is SARS-CoV-2 infection associated with increased risk of maternal mortality or serious morbidity from obstetric complications?

Findings: In this retrospective cohort study that included 14 104 patients, a composite outcome of maternal death or serious morbidity related to hypertensive disorders of pregnancy, postpartum hemorrhage, or infection other than SARS-CoV-2 occurred significantly more frequently in individuals with SARS-CoV-2 infection compared with individuals without SARS-CoV-2 infection (13.4% vs 9.2%, respectively).

Meaning: Among pregnant and postpartum individuals, SARS-CoV-2 infection was associated with increased risk of a composite outcome of maternal mortality or serious morbidity from obstetric complications."

JAMA: <u>Durability of Anti-Spike Antibodies in Infants After Maternal COVID-19 Vaccination or Natural Infection</u> (07 February 2022)

"We characterized the persistence of vaccine-induced maternal anti-S IgG in infant blood and compared persistence of infant anti-S IgG after maternal vaccination vs natural infection....

This study found that the majority of infants born to COVID-vaccinated mothers had persistent anti-S antibodies at 6 months, compared with infants born to mothers with SARS-CoV-2 infection. Understanding the persistence of maternal antibody levels in infants is important because COVID-19 infections in this age group account for a disproportionate burden of pediatric SARS-CoV-2—associated morbidity and because COVID-19 vaccines are not currently planned for administration to infants younger than 6 months."

# Pathological Analyses

Arch Pathol Lab Med: <u>Placental Tissue Destruction and Insufficiency from COVID-19 Causes</u>
<u>Stillbirth and Neonatal Death from Hypoxic-Ischemic Injury: A Study of 68 Cases with SARS-CoV-2 Placentitis from 12 Countries (10 February 2022)</u>

"Context: Perinatal death is an increasingly important problem as the COVID-19 pandemic continues, but the mechanism of death has been unclear.

Objective: To evaluate the role of the placenta in causing stillbirth and neonatal death following maternal infection with COVID-19 and confirmed placental positivity for SARS-CoV-2.

Design: Case-based retrospective clinico-pathological analysis by a multinational group of 44 perinatal specialists from 12 countries of placental and autopsy pathology findings from 64 stillborns and 4 neonatal deaths having placentas testing positive for SARS-CoV-2 following delivery to mothers with COVID-19.

Results: All 68 placentas had increased fibrin deposition and villous trophoblast necrosis and 66 had chronic histiocytic intervillositis, the three findings constituting SARS-CoV-2 placentitis. Sixty-three placentas had massive perivillous fibrin deposition. Severe destructive placental disease from SARS-CoV-2 placentitis averaged 77.7% tissue involvement. Other findings included multiple intervillous thrombi (37%; 25/68) and chronic villitis (32%; 22/68). The majority (19, 63%) of the 30 autopsies revealed no significant fetal abnormalities except for intrauterine hypoxia and asphyxia. Among all 68 cases, SARS-CoV-2 was detected from a body specimen in 16 of 28 cases tested, most frequently from nasopharyngeal swabs. Four autopsied stillborns had SARS-CoV-2 identified in internal organs.

Conclusions: The pathology abnormalities composing SARS-CoV-2 placentitis cause widespread and severe placental destruction resulting in placental malperfusion and insufficiency. In these cases, intrauterine and perinatal death likely results directly from placental insufficiency and fetal hypoxic-ischemic injury. There was no evidence that SARS-CoV-2 involvement of the fetus had a role in causing these deaths."

Emerg Infect Dis: <u>Detection of SARS-CoV-2 in Neonatal Autopsy Tissues and Placenta</u> (09 February 2022)

"Severe coronavirus disease in neonates is rare. We analyzed clinical, laboratory, and autopsy findings from a neonate in the United States who was delivered at 25 weeks of gestation and died 4 days after birth; the mother had asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and preeclampsia. We observed severe diffuse alveolar damage and localized SARS-CoV-2 by immunohistochemistry, in situ hybridization, and electron microscopy of the lungs of the neonate. We localized SARS-CoV-

2 RNA in neonatal heart and liver vascular endothelium by using in situ hybridization and detected SARS-CoV-2 RNA in neonatal and placental tissues by using reverse transcription PCR. Subgenomic reverse transcription PCR suggested viral replication in lung/airway, heart, and liver. These findings indicate that in utero SARS-CoV-2 transmission contributed to this neonatal death."

# **Pediatric Population**

# News in Brief

"Does Omicron hit kids harder? Scientists are trying to find out" (Nature).

"Pfizer and FDA pull back from plan to expedite review of Covid-19 vaccine in young children" (STAT).

Novavax said its two-dose COVID vaccine showed 80% efficacy in a phase III study involving adolescents and teenagers (Novavax).

#### Webinars and Other Events

WHAT: COVID-19 Updates: What Clinicians Need to Know About Multisystem

Inflammatory Syndrome in Children

WHEN: Thursday, 10 February 2022, 1400–1500 ET

OVERVIEW: "Multisystem inflammatory syndrome in children (MIS-C) is a rare but severe

condition associated with SARS-CoV-2 infection. The Centers for Disease Control

and Prevention (CDC) has been actively involved in MIS-C surveillance and

research, and development of MIS-C resources to support the public health and

healthcare community. During this COCA Call, presenters will discuss CDC's surveillance of MIS-C, updated MIS-C resources for healthcare providers, research that informed those resources, and data related to COVID-19

vaccination and MIS-C."

Includes free CE.

MORE INFO: https://emergency.cdc.gov/coca/calls/2022/callinfo 021022.asp

#### Journal Articles

MMWR: <u>Hospitalizations of Children and Adolescents with Laboratory-Confirmed COVID-19 — COVID-NET, 14 States, July 2021—January 2022</u> (18 February 2022)

"What is already known about this topic? COVID-19 can cause severe illness in children and adolescents.

What is added by this report? Coinciding with increased circulation of the Omicron variant, COVID-19—associated hospitalization rates among children and adolescents aged 0–17 years increased rapidly in late December 2021, especially among children aged 0–4 years who are not yet eligible for vaccination. Throughout the periods of Delta and Omicron predominance, hospitalization rates remained lower among fully vaccinated adolescents aged 12–17 years than among unvaccinated adolescents.

What are the implications for public health practice? Strategies to prevent COVID-19 among children and adolescents, including vaccination of eligible persons, are critical."

JAMA Pediatr: <u>Association of BNT162b2 COVID-19 Vaccination During Pregnancy With Neonatal and Early Infant Outcomes</u> (10 February 2022)

"Questions: Is prenatal exposure to maternal BNT162b2 messenger RNA COVID-19 vaccine associated with adverse outcomes at birth or early childhood?

Findings: In a population-based study including 24 288 singleton live births, the risks of preterm birth and small birth weight were similar between newborns prenatally exposed and unexposed to maternal vaccination.

Meaning: Maternal BNT162b2 vaccination in pregnancy was not associated with detrimental outcomes to the offspring."

JAMA Netw Open: <u>Characteristics</u>, <u>Outcomes</u>, <u>and Severity Risk Factors Associated With SARS-CoV-2 Infection Among Children in the US National COVID Cohort Collaborative</u> (08 February 2022)

"Question: What are the characteristics, changes over time, outcomes, and severity risk factors of children with SARS-CoV-2 within the National COVID Cohort Collaborative?

Findings: In this cohort study, 167 262 children at 56 sites were SARS-CoV-2—positive and 10 245 were hospitalized. Several demographic and comorbidity variables and many initial vital sign and laboratory test values were associated with higher peak illness severity.

Meaning: This study noted clinical data elements that could assist with early identification of children at risk for severe disease due to SARS-CoV-2 infection."

#### **Healthcare Workers**

## News in Brief

"For burned-out health workers, exhaustion from Covid-19 surges mixes with a sense of betrayal" (STAT).

#### Journal Articles

Front Psychiatry: <u>Companions in the Abyss: A Feasibility and Acceptability Study of an Online Therapy Group for Healthcare Providers Working During the COVID-19 Pandemic</u> (14 January 2022)

"Introduction: In the context of the global pandemic of the SARS-CoV-2 coronavirus (COVID-19), healthcare providers (HCPs) have experienced difficult moral and ethical dilemmas. Research is highlighting the importance of moral injury (MI)-a trauma syndrome related to transgressing personal morals and values-in understanding the psychological harm and occupational impairment experienced by HCPs. To date, MI treatments have largely been developed for military personnel and veterans and rely on in-person one-on-one psychotherapy.

Purpose: This project aims to explore the feasibility and acceptability of an evidence-informed online Acceptance and Commitment Therapy-based group therapy for MI in HCPs called "Accepting Moral Pain and Suffering for Healthcare Providers" (AMPS-HCP).

Method: This feasibility and acceptability study included three separate phases with the first two phases focused on the development of the psychotherapeutic intervention and the third phase focused on the evaluation of the psychotherapeutic intervention. Eight participants (including registered nurses, practical nurses and respiratory therapists) completed seven 90-min sessions in an online group format. The focus of these sessions included ACT and MI psychoeducation and experientials. Qualitative semi-structured interview data was thematically analyzed while demographic and quantitative self-reported outcome data underwent descriptive analysis and non-parametric testing.

Results: Results show that the intervention was highly feasible and acceptable to healthcare providers who worked on the frontline during COVID-19. Feasibility (referrals, eligibility, retention, participation engagement) was strong (8 out of 10 participants; 80% vs. desired >70% eligibility) and overall, 80% of participants completed 71% of the intervention. Data further supported the applicability and acceptability of the intervention. Preliminary data suggests that AMPS-HCP may supports HCPs to address MI.

Discussion: This study is the first to report on the development and evaluation of an online MI group intervention for registered nurses, registered practical nurses, and respiratory

therapists working during COVID-19. Results showed the use of both the online and group components of the intervention were acceptable and feasible during the third wave of COVID-19."

J Affect Disord: <u>Stressful events induce long-term gut microbiota dysbiosis and associated post-traumatic stress symptoms in healthcare workers fighting against COVID-19</u> (11 February 2022)

"Objective: The microbiota-gut-brain axis is a key pathway perturbed by prolonged stressors to produce brain and behavioral disorders. Frontline healthcare workers (FHWs) fighting against COVID-19 typically experience stressful event sequences and manifest some mental symptoms; however, the role of gut microbiota in such stress-induced mental problems remains unclear. We investigated the association between the psychological stress of FHW and gut microbiota.

Methods: We used full-length 16S rRNA gene sequencing to characterize the longitudinal changes in gut microbiota and investigated the impact of microbial changes on FHWs' mental status.

Results: Stressful events induced significant depression, anxiety, and stress in FHWs and disrupted the gut microbiome; gut dysbiosis persisted for at least half a year. Different microbes followed discrete trajectories during the half-year of follow-up. Microbes associated with mental health were mainly Faecalibacterium spp. and [Eubacterium] eligens group spp. with anti-inflammatory effects. Of note, the prediction model indicated that low abundance of [Eubacterium] hallii group uncultured bacterium and high abundance of Bacteroides eggerthii at Day 0 (immediately after the two-month frontline work) were significant determinants of the reappearance of post-traumatic stress symptoms in FHWs.

Limitations: The lack of metabolomic evidence and animal experiments result in the unclear mechanism of gut dysbiosis-related stress symptoms.

Conclusion: The stressful event sequences of fighting against COVID-19 induce characteristic longitudinal changes in gut microbiota, which underlies dynamic mental state changes."

# **Disparities and Health Equity**

# News in Brief

A recent issue of *Nature Human Behavior* focuses COVID-19 vaccine inequity. See: <a href="https://www.nature.com/collections/dgfibhcjeg">https://www.nature.com/collections/dgfibhcjeg</a>

## Journal Articles

JAMA Netw Open: <u>Comparison of Racial, Ethnic, and Geographic Location Diversity of</u>
<u>Participants Enrolled in Clinic-Based vs 2 Remote COVID-19 Clinical Trials</u> (14 February 2022)

"Question: Were racial, ethnic, and geographic location demographics of participants enrolled in 2 remote clinical trials with online recruitment more diverse compared with those of participants in a clinic-based COVID-19 study?

Findings: This cohort study was a secondary analysis of 1410 participants enrolled in 3 COVID-19 studies conducted in 2020 during the early COVID-19 pandemic and found that remote clinical trials with online recruitment had increased racial, ethnic, and geographic location diversity among study participants.

Meaning: These findings suggest that remotely conducted trials with inclusive social media recruitment may be considered as potential components to address insufficient representation and enrollment of diverse populations in clinical trials while continuing to research this important aspect of clinical trials."

Clin Infect Dis: <u>Social vulnerability and rurality associated with higher SARS-CoV-2 infection-induced seroprevalence</u>: a nationwide blood donor study, <u>United States</u>, <u>July 2020 – June 2021</u> (07 February 2022)

"Background: Most studies on health disparities during COVID-19 pandemic focused on reported cases and deaths, which are influenced by testing availability and access to care. This study aimed to examine SARS-CoV-2 antibody seroprevalence in the U.S. and its associations with race/ethnicity, rurality, and social vulnerability over time.

Methods: This repeated cross-sectional study used data from blood donations in 50 states and Washington, D.C. from July 2020 through June 2021. Donor ZIP codes were matched to counties and linked with Social Vulnerability Index (SVI) and urban-rural classification. SARS-CoV-2 antibody seroprevalences induced by infection and infection-vaccination combined were estimated. Association of infection-induced seropositivity with demographics, rurality, SVI, and its four themes were quantified using multivariate regression models.

Findings: Weighted seroprevalence differed significantly by race/ethnicity and rurality, and increased with increasing social vulnerability. During the study period, infection-induced seroprevalence increased from 1.6% to 27.2% and 3.7% to 20.0% in rural and urban counties, respectively, while rural counties had lower combined infection- and vaccination-induced seroprevalence (80.0% vs. 88.1%) in June 2021. Infection-induced seropositivity was associated with being Hispanic, non-Hispanic Black, and living in rural or higher socially vulnerable counties, after adjusting for demographic and geographic covariates.

Conclusion: The findings demonstrated increasing SARS-CoV-2 seroprevalence in the U.S. across all geographic, demographic, and social sectors. The study illustrated disparities by race-ethnicity, rurality, and social vulnerability. The findings identified areas for targeted vaccination strategies and can inform efforts to reduce inequities and prepare for future outbreaks."

PLoS One: <u>Persons tested for SAR-CoV-2 at a military treatment facility in Hawaii</u> (04 February 2022)

"Health inequalities based on race are well-documented, and the COVID-19 pandemic is no exception. Despite the advances in modern medicine, access to health care remains a primary determinant of health outcomes, especially for communities of color. African-Americans and other minorities are disproportionately at risk for infection with COVID-19, but this problem extends beyond access alone. This study sought to identify trends in racebased disparities in COVID-19 in the setting of universal access to care. Tripler Army Medical Center (TAMC) is a Department of Defense Military Treatment Facility (DoD-MTF) that provides full access to healthcare to active duty military members, beneficiaries, and veterans. We evaluated the characteristics of individuals diagnosed with SARS-CoV-2 infection at TAMC in a retrospective, case-controlled (1:1) study. Most patients (69%) had received a COVID-19 test within 3 days of symptom onset. Multivariable logistic regression analyses were used to identify factors associated with testing positive and to estimate adjusted odds ratios. African-American patients and patients who identified as "Other" ethnicities were two times more likely to test positive for SARS-CoV-2 relative to Caucasian patients. Other factors associated with testing positive include: younger age, male gender, previous positive test, presenting with >3 symptoms, close contact with a COVID-19 positive patient, and being a member of the US Navy. African-Americans and patients who identify as "Other" ethnicities had disproportionately higher rates of positivity of COVID-19. Although other factors contribute to increased test positivity across all patient populations, access to care does not appear to itself explain this discrepancy with COVID-19."

JAMA Psychiatry: <u>Multivariate, Transgenerational Associations of the COVID-19 Pandemic Across Minoritized and Marginalized Communities</u> (09 February 2022)

"Question: What baseline pre—COVID-19 pandemic household factors are associated with COVID-19 experiences as reported by approximately 10 000 children and their parents?

Findings: In this study of 9267 youth-parent dyads, of more than 17 000 variables, social determinants of inequity, including household income and family structure, emerged as the primary correlates of negative COVID-19 experiences, including increased difficulties with school among children and concerns over racism associated with the COVID-19 pandemic among parents.

Meaning: Community-level, transgenerational intervention strategies may be needed to combat the disproportionate burden of pandemics on minoritized and marginalized racial and ethnic populations."

MMWR: <u>COVID-19 Vaccination Coverage and Vaccine Confidence by Sexual Orientation and</u> Gender Identity — United States, August 29–October 30, 2021 (04 February 2022)

"What is already known about this topic? Lesbian, gay, bisexual, and transgender (LGBT) persons are at increased risk for severe COVID-19 illness because of a higher prevalence of comorbidities.

What is added by this report? COVID-19 vaccination coverage and vaccine confidence were higher among gay or lesbian adults than among heterosexual adults and higher among gay men than gay or lesbian women. There were no significant differences in vaccination coverage among persons based on gender identity. Vaccination coverage was lowest among non-Hispanic Black LGBT persons across all categories of sexual orientation and gender identity.

What are the implications for public health practice? To prevent serious illness and death, all persons in the United States, including those in the LGBT community, should stay up to date with recommended COVID-19 vaccinations."

#### **Mental Health and Wellness**

## **News in Brief**

"Ready for another pandemic malady? It's called 'decision fatigue'" (KHN).

#### **Journal Articles**

BMJ: Risks of mental health outcomes in people with covid-19: cohort study (16 February 2022)

"Objective: To estimate the risks of incident mental health disorders in survivors of the acute phase of covid-19.

Participants: Cohort comprising 153 848 people who survived the first 30 days of SARS-CoV-2 infection, and two control groups: a contemporary group (n=5 637 840) with no evidence of SARS-CoV-2, and a historical control group (n=5 859 251) that predated the covid-19 pandemic.

Main outcomes measures: Risks of prespecified incident mental health outcomes, calculated as hazard ratio and absolute risk difference per 1000 people at one year, with corresponding 95% confidence intervals. Predefined covariates and algorithmically selected high dimensional covariates were used to balance the covid-19 and control groups through inverse weighting.

Results: The covid-19 group showed an increased risk of incident anxiety disorders (hazard ratio 1.35 (95% confidence interval 1.30 to 1.39); risk difference 11.06 (95% confidence interval 9.64 to 12.53) per 1000 people at one year), depressive disorders (1.39 (1.34 to 1.43); 15.12 (13.38 to 16.91) per 1000 people at one year), stress and adjustment disorders (1.38 (1.34 to 1.43); 13.29 (11.71 to 14.92) per 1000 people at one year), and use of antidepressants (1.55 (1.50 to 1.60); 21.59 (19.63 to 23.60) per 1000 people at one year) and benzodiazepines (1.65 (1.58 to 1.72); 10.46 (9.37 to 11.61) per 1000 people at one year). The risk of incident opioid prescriptions also increased (1.76 (1.71 to 1.81); 35.90 (33.61 to 38.25) per 1000 people at one year), opioid use disorders (1.34 (1.21 to 1.48); 0.96 (0.59 to 1.37) per 1000 people at one year), and other (non-opioid) substance use disorders (1.20 (1.15 to 1.26); 4.34 (3.22 to 5.51) per 1000 people at one year). The covid-19 group also showed an increased risk of incident neurocognitive decline (1.80 (1.72 to 1.89); 10.75 (9.65 to 11.91) per 1000 people at one year) and sleep disorders (1.41 (1.38 to 1.45); 23.80 (21.65 to 26.00) per 1000 people at one year). The risk of any incident mental health diagnosis or prescription was increased (1.60 (1.55 to 1.66); 64.38 (58.90 to 70.01) per 1000 people at one year). The risks of examined outcomes were increased even among people who were not admitted to hospital and were highest among those who were admitted to hospital during the acute phase of covid-19. Results were consistent with those in the historical control group. The risk of incident mental health disorders was consistently higher in the covid-19 group in comparisons of people with covid-19 not admitted to hospital versus those not admitted to hospital for seasonal influenza, admitted to hospital with covid-19 versus admitted to hospital with seasonal influenza, and admitted to hospital with covid-19 versus admitted to hospital for any other cause.

Conclusions: The findings suggest that people who survive the acute phase of covid-19 are at increased risk of an array of incident mental health disorders. Tackling mental health disorders among survivors of covid-19 should be a priority."

Psychol Trauma: <u>Doomscrolling During COVID-19: The Negative Association Between Daily Social and Traditional Media Consumption and Mental Health Symptoms During the COVID-19 Pandemic</u> (14 February 2022)

"Objective: Consumption of traditional and social media markedly increased at the start of the COVID-19 pandemic as new information about the virus and safety guidelines evolved. Much of the information concerned restrictions on daily living activities and the risk posed by the virus. The term doomscrolling is used to describe the phenomenon of elevated

negative affect after viewing pandemic-related media. The magnitude and duration of this effect, however, is unclear. Furthermore, the effect of doomscrolling likely varies based on prior vulnerabilities for psychopathology, such as a history of childhood maltreatment. It was hypothesized that social and traditional media exposure were related to an increase in depression and PTSD and that this increase was moderated by childhood maltreatment severity.

Method: Participants completed a baseline assessment for psychopathology and 30 days of daily assessments of depression, PTSD, and pandemic-related media use.

Results: Using multilevel modeling, social media exposure was associated with increased depression and PTSD. This association was stronger for those with more severe maltreatment histories. Furthermore, those with more severe baseline psychopathology used more social media during this period. These relations were not observed for traditional media sources.

Conclusions: These results suggest that regular viewing of pandemic-related social media is associated with increases in psychopathology for those with existing vulnerabilities. Those with such vulnerabilities should adopt strategies to limit social media consumption."

# Other Infectious Diseases and Public Health Threats

# News in Brief

The Advisory Committee on Immunization Practices has published updated immunization schedules for adults (MMWR) and in children and adolescents (MMWR).

Drug-resistant malaria is emerging in Africa. Is the world ready?" (Undark)

Public Health Vaccines has initiated the first clinical trial for its single dose Nipah virus vaccine (PRNewswire).

"The hidden epidemic — antibiotic resistance is approaching a crisis point, and the world needs to act" (<u>Vox</u>).

<sup>&</sup>quot;Just 14 cases: Guinea worm disease nears eradication" (Nature).

<sup>&</sup>quot;APHIS announces final strategic framework for enhancing surveillance for SARS-CoV-2 and other emerging diseases under the American Rescue Plan" (<u>USDA</u>).

#### **Journal Articles**

Clin Infect Dis: <u>Sexually Transmitted Infection Transmission Dynamics During the Coronavirus</u>
<u>Disease 2019 (COVID-19) Pandemic Among Urban Gay, Bisexual, and Other Men Who Have Sex</u>
<u>With Men</u> (09 February 2022)

"Background: The impact of coronavirus disease 2019 (COVID-19) mitigation measures on sexually transmitted infection (STI) transmission and racial disparities remains unknown. Our objectives were to compare sex and drug risk behaviors, access to sexual health services, and STI positivity overall and by race during the COVID-19 pandemic compared with pre-pandemic among urban sexual minority men (MSM).

Methods: Sexually active MSM aged 18-45 years were administered a behavioral survey and STI testing every 3-months. Participants who completed at least 1 during-pandemic (April 2020-December 2020) and 1 pre-pandemic study visit (before 13 March 2020) that occurred less than 6 months apart were included. Regression models were used to compare during-and pre-pandemic visit outcomes

Results: Overall, among 231 MSM, reports of more than 3 sex partners declined(pandemic-1: adjusted prevalence ratio 0.68; 95% confidence interval: .54-.86; pandemic-2: 0.65, .51-.84; pandemic-3: 0.57, .43-.75), substance use decreased (pandemic-1: 0.75, .61-.75; pandemic-2: 0.62, .50-.78; pandemic-3: 0.61, .47-.80), and human immunodeficiency virus/preexposure prophylaxis care engagement (pandemic-1: 1.20, 1.07-1.34; pandemic-2: 1.24, 1.11-1.39; pandemic-3: 1.30, 1.16-1.47) increased. STI testing decreased (pandemic-1: 0.68, .57-.81; pandemic-2: 0.78, .67-.92), then rebounded (pandemic-3: 1.01, .87-1.18). Neither Chlamydia (pandemic-2: 1.62, .75-3.46; pandemic-3: 1.13, .24-1.27) nor gonorrhea (pandemic-2: 0.87, .46 1.62; pandemic-3: 0.56, .24-1.27) positivity significantly changed during vs pre-pandemic. Trends were mostly similar among Black vs. non-Black MSM.

Conclusions: We observed sustained decreases in STI risk behaviors but minimal change in STI positivity during compared with pre-pandemic. Our findings underscore the need for novel STI prevention strategies that can be delivered without in-person interactions."

Sci Transl Med: <u>Ebola virus persistence and disease recrudescence in the brains of antibody-treated nonhuman primate survivors</u> (09 February 2022)

"Effective therapeutics have been developed against acute Ebola virus disease (EVD) in both humans and experimentally infected nonhuman primates. However, the risk of viral persistence and associated disease recrudescence in survivors receiving these therapeutics remains unclear. In contrast to rhesus macaques that survived Ebola virus (EBOV) exposure in the absence of treatment, we discovered that EBOV, despite being cleared from all other organs, persisted in the brain ventricular system of rhesus macaque survivors that had received monoclonal antibody (mAb) treatment. In mAb-treated macaque survivors, EBOV

persisted in macrophages infiltrating the brain ventricular system, including the choroid plexuses. This macrophage infiltration was accompanied by severe tissue damage, including ventriculitis, choroid plexitis, and meningoencephalitis. Specifically, choroid plexus endothelium-derived EBOV infection led to viral persistence in the macaque brain ventricular system. This resulted in apoptosis of ependymal cells, which constitute the blood-cerebrospinal fluid barrier of the choroid plexuses. Fatal brain-confined recrudescence of EBOV infection manifested as severe inflammation, local pathology, and widespread infection of the ventricular system and adjacent neuropil in some of the mAbtreated macaque survivors. This study highlights organ-specific EBOV persistence and fatal recrudescent disease in rhesus macaque survivors after therapeutic treatment and has implications for the long-term follow-up of human survivors of EVD."

PLoS Negl Trop Dis: <u>Paving the way for human vaccination against Rift Valley fever virus: A systematic literature review of RVFV epidemiology from 1999 to 2021</u> (24 January 2022)

"Background: Rift Valley fever virus (RVFV) is a lethal threat to humans and livestock in many parts of Africa, the Arabian Peninsula, and the Indian Ocean. This systematic review's objective was to consolidate understanding of RVFV epidemiology during 1999-2021 and highlight knowledge gaps relevant to plans for human vaccine trials.

Methodology/principal findings: The review is registered with PROSPERO (CRD42020221622). Reports of RVFV infection or exposure among humans, animals, and/or vectors in Africa, the Arabian Peninsula, and the Indian Ocean during the period January 1999 to June 2021 were eligible for inclusion. Online databases were searched for publications, and supplemental materials were recovered from official reports and research colleagues. Exposures were classified into five groups: 1) acute human RVF cases, 2) acute animal cases, 3) human RVFV sero-surveys, 4) animal sero-surveys, and 5) arthropod infections. Human risk factors, circulating RVFV lineages, and surveillance methods were also tabulated. In meta-analysis of risks, summary odds ratios were computed using random-effects modeling. 1104 unique human or animal RVFV transmission events were reported in 39 countries during 1999-2021. Outbreaks among humans or animals occurred at rates of 5.8/year and 12.4/year, respectively, with Mauritania, Madagascar, Kenya, South Africa, and Sudan having the most human outbreak years. Men had greater odds of RVFV infection than women, and animal contact, butchering, milking, and handling aborted material were significantly associated with greater odds of exposure. Animal infection risk was linked to location, proximity to water, and exposure to other herds or wildlife. RVFV was detected in a variety of mosquito vectors during interepidemic periods, confirming ongoing transmission.

Conclusions/significance: With broad variability in surveillance, case finding, survey design, and RVFV case confirmation, combined with uncertainty about populations-at-risk, there were inconsistent results from location to location. However, it was evident that RVFV

transmission is expanding its range and frequency. Gaps assessment indicated the need to harmonize human and animal surveillance and improve diagnostics and genotyping. Given the frequency of RVFV outbreaks, human vaccination has strong potential to mitigate the impact of this now widely endemic disease."

## **Statistics**

	Total Cases	Total Deaths	
Global	420,253,315	5,865,558	
<b>United States</b>	78,273,641	931,769	
	1111 CCCC		

JHU CSSE as of 1	1000 ET 18	Februar	y 2022
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	Total	Hospitalization	Death		
	Cases	Cumulative	Cumulative		
		Count	Count		
Virginia	1,622,685	47,140	18,016		
Chesapeake	48,851	1,362	436		
Hampton	27,026	723	283		
Newport News	35,644	945	357		
Norfolk	40,908	1,739	438		
Portsmouth	20,458	1,065	296		
Suffolk	18,406	784	275		
Virginia Beach	87,908	3,727	743		
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